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22 UNITED STATES DISTRICT COURT
23 SOUTHERN DISTRICT OF CALIFORNIA

24 GEN-PROBE INCORPORATED,

25 Plaintiff,

26 v.

27 VYSIS, INC.,

28 Defendant.

No. 99CV2668 H (AJB)

NOTICE OF MOTION AND MOTION OF GEN-
PROBE INCORPORATED FOR PARTIAL
SUMMARY JUDGMENT

Date: May 29, 2001
Time: 10:30 a.m.
Dept.: Courtroom 1

29 TO ALL PARTIES AND THEIR ATTORNEYS OF RECORD HEREIN:

30 PLEASE TAKE NOTICE that on March 29, 2001 at 10:30 a.m. in Courtroom 1 of the above
31 entitled court located at the United States Courthouse, 940 Front Street, San Diego, California
32 92101, plaintiff Gen-Probe Incorporated ("Gen-Probe") will and hereby does move the Court
33 under Federal Rule of Civil Procedure, Rule 56 for partial summary judgment under Counts One

1 and Three of its Second Amended Complaint that its nucleic acid test for human
2 immunodeficiency virus ("HIV") and hepatitis C virus ("HCV") does not literally infringe the
3 claims of U.S. Patent No. 5,750,338 (the "'338 patent"). The grounds of this motion are that there
4 is no disputed issue of material fact that Gen-Probe's HIV and HCV test kit does not contain each
5 of the claim limitations of the '338 patent and thus does not infringe that patent. In particular, the
6 methods and kits claimed in the '338 patent are limited to using only non-specific amplification
7 methods. Gen-Probe's HIV and HCV test kit, on the other hand, uses a method of specific
8 amplification.

9 This Motion is based on this Notice of Motion and Motion, the accompanying
10 Memorandum of Points and Authorities, the Declaration of R. William Bowen, the Declaration of
11 Dr. Joseph O. Falkinham III, Ph.D., the Declaration of Dr. Matthew Longiaru, the Notice of
12 Lodgment of Exhibits, and on such other and further oral and documentary evidence as the Court
13 may consider at the time of the hearing.

14 Dated: April 30, 2001

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14 UNITED STATES DISTRICT COURT

16 SOUTHERN DISTRICT OF CALIFORNIA

17 GEN-PROBE INCORPORATED,

18 Plaintiff,

19 v.

20 VYSIS, INC.,

21 Defendant.

No. 99cv2668 H (AJB)
JUDGE MARILYN L. HUFF

MEMORANDUM OF POINTS AND AUTHORITIES
IN SUPPORT OF PLAINTIFF GEN-PROBE
INCORPORATED'S MOTION FOR PARTIAL
SUMMARY JUDGMENT

DATE: May 29, 2001
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DEPT: Courtroom 1

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1 I. INTRODUCTION

2 Plaintiff Gen-Probe moves for partial summary judgment under Counts One and Three of
3 its Second Amended Complaint that its nucleic acid test for human immunodeficiency virus
4 ("HIV") and hepatitis C virus ("HCV") does not literally infringe the claims of U.S. Patent No.
5 5,750,338 ("the '338 Patent")¹. Gen-Probe's HIV/HCV test is used to screen donated blood using
6 a novel and highly sensitive technology that "amplifies" even a small amount of virus in a sample
7 to a level where it can be detected, using Gen-Probe's own patented method of "Transcription-
8 Mediated Amplification" or "TMA."

9 Gen-Probe's TMA amplification process uses "primers" that attach to carefully selected
10 portions (or "sequences") of the target organism's nucleic acids. These sequence-specific primers
11 are carefully researched and designed to attach to unique nucleic acids of the target organism, so
12 that the test produces accurate results. The single issue presented by this motion is whether the
13 claims of the '338 patent encompass nucleic acid amplification methods such as TMA, which use
14 sequence-specific primers. By this motion, Gen-Probe shows that the claims of the '338 patent in
15 fact encompass only amplification methods using *non-specific* primers and enzymes. Therefore
16 the claims of the patent do not encompass Gen-Probe's TMA products, and summary judgment
17 should be granted.

18 As discussed below, the scope of the patent claims is determined primarily from the face of
19 the patent. In this case, the result required by such analysis is confirmed by unequivocal additional
20 evidence. For example, on December 15, 1989, the Director of Business Development and
21 Licensing for Gene-Trak Systems (the predecessor to defendant Vysis, Inc.) clearly described the
22 invention of the '338 patent:

23 Cetus, Sibia, Salk, Biotechnica, etc. [e.g., other amplification
24 methods] all claim **specific** primers for amplification, whereas the
25 present invention claims use of the opposite, namely, **non-specific**
26 primers or promoters.

(Exhibit 1 at page 2, emphasis in original).

27 ¹ The '338 Patent is attached as Exhibit 8 to Gen-Probe's accompanying Notice of Lodgment of
28 Exhibits. Unless otherwise specified, all references to exhibits refer to exhibits lodged with such
Notice.

1 Section I of this memorandum sets forth scientific background intended to assist the Court
2 in its analysis of the case. In Section II of the memorandum, Gen-Probe shows that the '338 patent
3 must be construed to cover only non-specific amplification, based on:

- 4 1. An analysis of the patent itself, which clearly describes only non-specific
5 amplification methods and states that sequence-specific primers are not necessary
6 when the methods of the patent are used;
- 7 2. The expert declaration of Joseph O. Falkinham, III, Ph.D.;
- 8 3. Documents and testimony that clearly establish the inventors' and the patents
9 owner's admissions as to scope of the patent claims.

10 Finally, in section III of the memorandum, Gen-Probe shows that its HIV/HCV test does not
11 literally infringe² the claims of the '338 patent, properly construed.

12 II. SCIENTIFIC BACKGROUND

13 The '338 patent relates generally to methods for use in nucleic acid diagnostics, including
14 the use of nucleic acid "probes" to detect infectious organisms. In particular, the patent relates to
15 methods by which nucleic acids may be "captured" onto solid supports and copied (or
16 "amplified"), so that small quantities of these nucleic acids may be then detected by probes.

17 In order to construe the claims of the '338 patent, a very basic familiarity with nucleic acid
18 amplification is required. In particular, it is necessary to understand the distinction between
19 "specific" and "non-specific" primers and enzymes, used in the amplification process to mark the
20 nucleic acid sequences to be copied. A brief overview of the relevant technology is set forth in
21 this section.

22 ///

23 ///

24 ² Several inconsequential distinctions arise in this case from the fact that Gen-Probe has licensed
25 the '338 patent. First, because this is a declaratory judgment action brought by Gen-Probe, the
26 plaintiff-defendant positions are reversed from a typical infringement suit. Thus, the patent owner,
27 Vysis, is the defendant. Second, despite the fact that plaintiff Gen-Probe holds a license to the
28 '338 patent and cannot technically be found to "infringe" the '338 patent, the legal issue of
infringement is central to Counts One and Three of Gen-Probe's Second Amended Complaint. For
example, the terms of the license impose obligations only upon those products of Gen-Probe that
would constitute an infringement of the '338 patent but for the license. For the sake of
convenience and familiarity, this motion uses the same terminology applicable to a suit for patent
infringement.

1 **A. Nucleic Acids**

2 Nucleic acids are molecules that store and transfer genetic information in all living
3 organisms. The two main types of nucleic acids are DNA (deoxyribonucleic acid) and RNA
4 (ribonucleic acid). DNA functions as a stable repository of genetic information, while RNA
5 typically serves to transfer the information stored within DNA to the cell's machinery for making
6 proteins.

7 DNA and RNA are both composed of chains of chemical sub-units called "nucleotides."
8 Each nucleotide has three components: a sugar ("deoxyribose"), a phosphate group, and a "base"
9 containing nitrogen. There are four types of nucleotides in DNA, each of which has a different
10 base: adenine, thymine, guanine, or cytosine (abbreviated A, T, G, and C). These four "bases"
11 form the building blocks of all DNA³. The sugar and phosphate groups within each nucleotide
12 form the backbone of the DNA molecule, linking together the individual nucleotides that make up
13 the molecule. (See Illustration, Exhibit 2).

14 The "sequence" of the individual A, T, G, and C nucleotides in a DNA molecule encodes
15 the genetic information that instructs the cell how to make particular proteins. Because DNA
16 sequences determine which proteins a cell will make, it is differences in their DNA sequences that
17 make the cells of one organism differ from the cells of another.

18 DNA in cells ordinarily occurs in a molecular structure in which two "strands" of DNA are
19 specifically bound to one another. Double-stranded DNA is often depicted as a ladder in which
20 each strand forms one side of the ladder and one half of a rung of the ladder. Each nucleotide's
21 base is chemically bonded to a nucleotide base on the opposite strand to form the rungs of the
22 ladder. In its normal state, the ladder is twisted spirally, forming a three-dimensional "double
23 helix" structure. (See Illustration, Exhibit 3).

24 ///

25 _____
26 ³ RNA also consists of a sequence of four bases comprised of four different nucleotides. The four
27 nucleotides contained in RNA are identical to DNA except that thymine (T) is replaced by uracil
28 (U). Unlike DNA, RNA typically exists as a single strand. However, the nucleotides of RNA
have a similar attraction to complementary nucleotides (A binding to U, and C binding to G) and
two RNA molecules, or an RNA and a DNA molecule, can form a double helix in which the two
strands are joined by complementary base pairing.

1 In double-stranded DNA, the nucleotides on opposite sides of the ladder are always paired
2 in a precise way. An "A" nucleotide binds only to a "T" nucleotide on the opposite strand, and
3 vice versa. Likewise, a "G" nucleotide binds only to a "C" nucleotide, and vice versa. (See
4 Illustration, Exhibit 4.)

5 Each combination of an "A" nucleotide with a "T" nucleotide (or a "C" with a "G") is
6 referred to as a "base pair." The way in which each type of nucleotide binds only to one other type
7 of nucleotide is called "complementary base pairing." As a result of complementary base pairing,
8 the sequence of nucleotides on one strand of a DNA molecule necessarily determines the sequence
9 of nucleotides on the opposite strand.

10 B. Nucleic Acid Probes

11 The "attraction" of a nucleotide sequence to its "complementary" sequence allows a
12 scientist to use pieces of nucleic acid as "probes" to detect the presence of a target nucleic acid in a
13 test sample. If two complementary pieces of DNA (or RNA) are present in a solution under the
14 right conditions, the complementary bases will come together and bind to form double strands.
15 This method is commonly known as "nucleic acid hybridization." Nucleic acid hybridization
16 techniques can be applied in a diagnostic test to detect an infectious organism (the "target"
17 organism) by the use of a probe that is designed to bind specifically to a nucleic acid sequence that
18 is known to be unique to the target organism. The sample suspected of containing the infectious
19 organism is treated to break open the organism, release its nucleic acids into the solution, and
20 render them single-stranded, if necessary. The specific probe is then added, and conditions
21 conducive to hybridization are established. (See Illustration, Exhibit 5.)

22 In theory, if the target organism is present in the sample, the "probe" should bind to the
23 target organism's nucleic acids because the sequence of the probe has been designed to be
24 complementary to them. By attaching a detectable "label" to a probe, scientists are able to
25 determine how much, if any, probe has bound to sequences from the target organism.

26 Nucleic acid probes are generally designed based on the fact that each species of organism
27 has its own unique genome. By the early 1980's, scientists were routinely determining the specific
28 nucleotide sequences of different species' DNA and RNA and searching for sequences that were

1 common to and different among various organisms. Using this information, scientists could
2 design probes that, under the right conditions, would bind to nucleic acid sequences characteristic
3 of a specific target organism and not to sequences of other organisms.

4 However, related species have substantial portions of their DNA that are identical.
5 Generally, more closely related species have more DNA sequences in common. DNA sequences
6 that are common to a target organism and other organisms can interfere with the specific detection
7 of the desired target. For example, the sequence CGTAG shown in the Illustration of Exhibit 2
8 might appear in the DNA of many species. A probe that is complementary to this sequence would
9 bind to the DNA of the target organism, and also to the DNA of other species that contain the same
10 sequence. Samples that did not contain the target organism, but did contain one or more of the
11 other species, would be falsely analyzed if such a probe were to be used in a diagnostic test.

12 Thus, it is desirable to have a probe that binds only to DNA of the target pathogen and not
13 to DNA contained in other organisms. A probe that consists of a DNA sequence unique to the
14 target organism and which therefore binds exclusively to the DNA of the target organism, and not
15 to DNA of other organisms, is said to be "specific" for the target organism.

16 C. Target Capture

17 Target capture techniques are used in nucleic acid methods to isolate a particular
18 nucleic acid of interest prior to detection or other steps. In target capture methods, the target
19 nucleic acid is bound to a solid support, such as a filter, particle, or a bead, which allows the target
20 to be removed from the sample in which it was originally contained. The immobilized target
21 nucleic acid is directly detected with a probe, amplified prior to detection, or used for other
22 purposes.

23 The target nucleic acid can be immobilized on the solid support either by direct attachment
24 or by the use of an intermediate "capture probe." A capture probe is a nucleic acid sequence that is
25 designed to bind with the target organism's DNA or RNA and also attach to the solid support (See
26 Illustration, Exhibit 6).

27 ///

28 ///

1 **D. Amplification**

2 Often, it is necessary to detect very small numbers of infectious organisms in a
3 sample. This is particularly true when screening for the presence of the organism in the absence of
4 a full-blown infection. Examples include screening blood intended for transfusion for the presence
5 of viruses such as HIV. In these situations, the presence of even small numbers of organisms may
6 lead to the transmission of infection from one individual to another.

7 Scientists have long understood that detection of a small number of organisms in a sample
8 requires that the number of "target" organisms be increased in number in order to achieve a
9 detectable level. There are many ways to accomplish this. For example, one classic way to detect
10 low numbers of organisms is to transfer the sample to culture media that will support the growth of
11 the organism. After a suitable time, the number of organisms will generally have increased
12 sufficiently to allow them to be detected directly by hybridization or other methods.

13 A faster approach is to increase the target organism's nucleic acid through processes
14 known as "nucleic acid amplification." Amplification procedures are generally performed with
15 enzymes and primers. Enzymes are protein molecules that catalyze biological reactions.
16 "Polymerase" enzymes are used to copy a DNA or RNA strand to make its complement. Such
17 naturally occurring enzymes are normally used in cellular processes to make copies of the
18 organism's genes to be passed on to its progeny.

19 Scientists have learned to use enzymes such as polymerase to increase the amount of a
20 DNA or RNA in a sample up to a billion-fold. By making copies of the target organism's nucleic
21 acids, the amount of target that is available to bind with a probe in a detection step is increased to
22 easily detected levels. One of the most famous amplification techniques is the "polymerase chain
23 reaction" (PCR), which uses DNA polymerase and specific primers to multiply specific nucleotide
24 sequences within a nucleic acid. Dr. Kary Mullis received the Nobel Prize in chemistry for his
25 1983 invention of PCR.

26 "Primers" are short pieces of DNA that are used in amplification methods to cause an
27 enzyme such as DNA polymerase to start its copying action at a certain point along a nucleic acid
28 sequence. Like probes in the detection step, primers work by binding (hybridizing) to a

1 complementary nucleotide sequence in the target nucleic acid. DNA polymerase then copies the
2 target nucleic acid beginning at the point where the primer attached. (See Illustration, Exhibit 7.)
3 The procedure can be repeated many times, resulting in copies of the copies. This process of
4 "geometric" or "exponential" amplification produces millions of copies of the target segment that
5 is bounded by the sites where the primers attached.

6 Primers used in amplification processes can be either specific or non-specific. "Specific"
7 primers are carefully designed to bind only to a pre-selected nucleic acid sequence of a particular
8 target organism, usually a sequence selected to be unique to that organism. Non-specific or
9 "random" primers can be used with DNA polymerases to copy random portions of the nucleic acid
10 sequence of the target organism. When random primers are used, the resulting amplification
11 process is referred to as "non-specific" because DNA synthesis begins at random locations all over
12 the target nucleic acid and any other nucleic acids that may be present in the sample are also
13 amplified. Using random, non-specific primers avoids the work required to select, make, and test
14 specific primers for each individual target organism.

15 Another form of enzymatic amplification makes copies of RNA from a DNA sequence
16 using an enzyme called "transcriptase." Transcriptases are types of polymerase that make an RNA
17 sequence that is complementary to an initial DNA sequence. The process of making this RNA
18 copy ("transcription") may also be specific or non-specific. Transcriptases do not use primers but
19 instead begin RNA synthesis at special DNA sequences ("promoter sequences"). Many
20 transcriptases only carry out specific transcription in the presence of other special protein factors
21 (often called "subunits"). In the absence of these subunits, the "core" transcriptase enzyme binds
22 randomly to the DNA and starts making RNA molecules at multiple random sites.

23 **III. THE CLAIMS OF THE '338 PATENT MUST BE LIMITED TO NON-SPECIFIC** 24 **AMPLIFICATION METHODS**

25 By this motion, Gen-Probe moves for summary judgment on the issue of literal
26 infringement inherent in Counts One and Three of the Second Amended Complaint. A
27 determination of the issue of infringement involves a two-step analysis. First, the Court must
28 construe the claims at issue in order to determine their meaning and scope. Second, the Court

1 must determine whether the claims, as properly construed, encompass the technology used by
2 Gen-Probe. *WMS Gaming Inc. v. International Game Technology*, 184 F.3d 1339, 1346 (Fed. Cir.
3 1999); *Zelinski v. Brunswick Corp.*, 185 F.3d 1311, 1315 (Fed. Cir. 1999). The first step of the
4 Court's analysis, construction of the claims, often decides the question of infringement. *Netword*
5 *LLC v. Centraal Corp.*, 242 F.3d 1347, 1350 (Fed. Cir. 2001).

6 Claim construction, the judicial statement of what is and is not covered by the technical
7 terms and other words of the claims, is a question of law to be decided by the Court alone.
8 *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370
9 (1996). The focus of the Court's inquiry in claim construction is on the objective test of what one
10 of ordinary skill in the art would have understood the terms used in the patent claims to mean, as
11 of the date the patent application was filed.⁴ *Id* at 985-86.

12 In determining the proper construction of a claim, the Court has numerous sources that it
13 may properly utilize for guidance. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582
14 (Fed. Cir. 1996). These sources include both "intrinsic" evidence (e.g., the patent specification)
15 and "extrinsic" evidence (e.g., expert testimony and the inventor's/patent owner's own
16 descriptions of the invention). *Id*.

17 The starting point for any claim construction is the patent claim itself. *Pitney Bowes, Inc.*
18 *v. Hewlett Packard Co.*, 182 F.3d 1298, 1305 (Fed. Cir. 1999). However, "claims are always
19 construed in light of the specification, of which they are a part." *Netword*, 242 F.3d at 1352.
20 "The claims are directed to the invention that is described in the specification; they do not have
21 meaning removed from the context in which they arose." *Id.* at 1352; *Slimfold Mfg. Co. v.*
22 *Kinthead Indus., Inc.*, 810 F.2d 1113, 1116 (Fed. Cir. 1987) (claims are not interpreted "in a
23 vacuum," but are read and understood in light of the specification of which they are a part).

24 ///

25
26 ⁴ Gen-Probe submits that, for the purposes of this motion at least, any disagreement or dispute as
27 to the actual level and sophistication of the "person or ordinary skill" in 1987 is insubstantial at
28 best. As of 1987, all of the inventors held doctorate degrees in molecular biology or equivalent
technical disciplines. For the purpose of this motion, Gen-Probe will submit to that level of skill
as "ordinary" for the Court's purposes.

1 Thus, when a word or phrase in a claim is used in the specification, the relevant passages
2 must be considered in order to determine what the term means in the claim. *Renishaw PLC v.*
3 *Marposs Societa' Per Azioni*, 158 F.3d 1243, 1248 (Fed. Cir. 1998). It is *always* necessary to
4 review the patent specification as part of the claim construction process. *United States v. Adams*,
5 383 U.S. 39, 49 (1966) (claims are to be construed in light of the specifications and both are to be
6 read with a view to ascertaining the invention); *Vitronics Corp.*, 90 F.3d at 1582; *Markman*, 52
7 F.3d at 979-80.

8 Ideally, the meaning of a term to one of ordinary skill in the art can be determined from the
9 face of the patent, *e.g.*, the intrinsic evidence. *Markman*, 52 F.3d at 979-80. While the Court's
10 primary focus is on the patent specification, reliable extrinsic evidence may also be considered:

11 [I]t is entirely appropriate, perhaps even preferable, for a court to
12 consult trustworthy extrinsic evidence to ensure that the claim
13 construction it is tending to form from the patent file is not
inconsistent with clearly expressed, plainly apposite, and widely held
understandings in the pertinent technical field.

14 *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1309, (Fed. Cir. 1999). In *Pitney*
15 *Bowes*, Judge Michel further pointed out:

16 While a judge is well-equipped to interpret the legal aspects of the
17 document, he or she must also interpret the technical aspects of the
18 document, and indeed its overall meaning, *from the vantage point of*
19 *one skilled in the art.* ... Although the patent file may often be
sufficient to permit the judge to interpret the technical aspects of the
patent properly, *consultation of extrinsic evidence is particularly*
20 *appropriate to ensure that his or her understanding of the technical*
aspects of the patent is not entirely at variance with the
understanding of one skilled in the art.

21 *Id.*, citing *Mantech Envtl. Corp. v. Hudson Envtl. Servs., Inc.*, 152 F.3d 1368, 1373 (Fed. Civ.
22 1998) (emphasis added). These principles guide the construction of the claims of the '338 patent⁵.

23 ///

24
25 ⁵ Gen-Probe's motion for summary judgment is based solely on the claim construction arguments
26 expressly set forth in this memorandum. Gen-Probe believes that the claims of the '338 patent
27 must also be limited to non-specific amplification on the basis of 35 U.S.C. § 112, paragraph six
(means-plus-function, step-plus-function). Gen-Probe reserves its arguments with respect to claim
28 construction pursuant to 35 U.S.C. § 112, paragraph six. Furthermore, Gen-Probe believes that the
parties dispute still other terms of the '338 patent that are not germane to the Court's resolution of
this motion.

1 **A. The Claims of the '338 Patent**

2 The '338 patent, Exhibit 8, consists of the specification, including drawings, and the
3 claims. The '338 patent contains six independent claims (claims 1, 7, 19, 27, 28 and 34). Each of
4 these claims is generally directed to a method of, or a kit for, amplifying and/or detecting a target
5 polynucleotide (i.e., a nucleic acid), wherein the target is first isolated on a support.

6 Each of the claims contains a step of "amplifying" the target polynucleotide or sample. For
7 example, claim 1 provides:

8 1. A method for amplifying a target polynucleotide contained in a sample
9 comprising the steps of:

10 (a) contacting the sample with a first support which binds to the target
11 polynucleotide;

12 (b) substantially separating the support and bound target polynucleotide from the
13 sample; and

14 (c) amplifying the target polynucleotide.

15 (Exhibit 8 at col. 32, ll. 27 to 33, emphasis added.) This motion concerns the proper construction
16 of the term "amplifying" as used in the claims of the '338 patent.

17 **B. The Teaching of the Patent**

18 The issue of what a skilled scientist would have understood the term "amplifying"
19 to mean is determined primarily from the specification of the patent. *Netword*, 242 F.3d at 2;
20 *Markman*, 52 F.3d at 979-80.

21 In the "Background of the Invention" section, the patent defines the term "amplify" in very
22 broad terms that encompass many different methods of amplification, including many that were
23 already well known in the prior art. Throughout the remainder of the specification, however, the
24 inventors teach only *non-specific* amplification because a suggested benefit of the invention is that
25 it *eliminates* the need to design and prepare specific primers and/or the need to use specific
26 enzymes.

27 Significantly, the specification sets forth four examples (Examples 4 through 7) of the
28 amplification methods taught by the inventors. Immediately before the first example that includes
an amplification step (Example 4), the inventors expressly set forth their teachings with respect to

1 amplification methods. Referring to the target capture methods described in Examples 1 through
2 3, the inventors stated:

3 The sensitivity of the above DNA or RNA target capture methods
4 can be enhanced by amplifying the captured nucleic acids. This can
5 be achieved by *nonspecific replication using standard enzymes*
(polymerases and/or transcriptases).

6 ('338 patent, Exh. 8, at col. 30, ll. 14-18, emphasis added.)

7 The inventors then made clear that the reference to non-specific amplification methods was
8 intentional and pointed out that one of the express benefits of their invention was that it permitted
9 the use of non-specific enzymes and non-specific primers:

10 Amplification of the target nucleic acid sequences, because it
11 follows purification of the target sequences, can employ **non-**
12 **specific** enzymes or primers. **Thus no specifically tailored primers**
13 **are needed for each test, and the same standard reagents can be**
14 **used, regardless of targets.**

15 (*Id.* at col. 30, ll. 30-40, emphasis added.) This teaching clearly expresses that a primary benefit of
16 the invention is the ability to use non-specific enzymes or primers, thereby avoiding the need to
17 craft specific primers for each particular target organism and the need to use other individualized
18 reagents such as specific transcriptases.

19 C. The Examples of the Patent

20 Immediately following the fundamental teaching of the '338 patent as set forth
21 above, the specification sets forth four examples of the amplification methods contemplated by the
22 inventors ('338 Patent, Exh. 8, col. 30, l. 43 to col. 32, l. 25, examples 4-7). Consistent with the
23 teaching of the patent that sequence-specific primers and specific enzymes are not necessary, each
24 example suggests and describes amplification methods that use only non-specific primers and
25 enzymes.

26 Example 4 illustrates "the use of RNA polymerase to amplify target DNA." ('338 Patent,
27 Exh. 8, at col. 30, ll. 44-45.) It describes a method for amplifying the capture DNA by non-
28 specific amplification using polymerases that lack transcriptional specificity. (*Id.* at col. 30, l. 59 -
col. 31, l.17). Example 4 discloses only non-specific amplification:

Q. So recapping the examples, examples one through three disclose
capture methods without amplification?

1 A. Yes.

2 Q. And example four discloses linear *nonspecific* amplification?

3 A. Yes.

4 (Lawrie Depo., Exh. 9, at 231:7-13, emphasis added.)

5 Example 5 also describes a non-specific amplification method in which that the target
6 DNA is replicated using random (*i.e.*, non-specific) primers and non-specific transcription of that
7 DNA into RNA:

8 In this example, both non-specific replication of target DNA and
9 transcription of that DNA are used to amplify capture target DNA...
10 Because the primers are *random*, some will, simple (*sic*) as a matter
of statistics, bind to and cause replication of sample sequences, no
matter what those sequences are. . . .

11 ('338 Patent, Exh. 8, at col. 31, ll. 24-54, emphasis added.) Example 5 discloses only non-specific
12 amplification. (Lawrie Depo., Exh. 9, at 231:14-16; Richards Depo., Exh. 10., at 139:23 – 140:3.)

13 Example 6 describes replication of target DNA using DNA polymerase and *random*
14 hexamer⁶ oligonucleotides "to bring about *non-specific* double-stranded DNA synthesis" ('338
15 Patent, Exh. 8, at col. 31, ll. 63-64), using a series of repeated heat denaturation and enzyme
16 replacement steps (*id.*, col. 31, l. 64 to col. 32, l. 19). Example 6 also discloses only *nonspecific*
17 amplification. (Lawrie Depo., Exh. 9, at 231:17-19; Richards Depo., Exh. 10, at 140:9-13.)

18 Finally, Example 7 describes *non-specific* amplification using an RNA polymerase, Q β
19 replicase:

20 In this example, rRNA and RNA transcribed from target DNA is
21 purified using a capture probe, described above. The hybrid duplex
22 is then denatured and single stranded nucleic acids are then
replicated *non-specifically* using Q β replicase...

23 ('338 Patent, Exh. 8, at col. 32, l. 10-19.) Example 7 discloses only nonspecific amplification.
24 (Lawrie Depo., Exh. 9, at 231:20-22; Richards Depo., Exh. 10, at 141: 3-7.)

25 ///

26
27 ⁶ Certain of the examples and drawings refer to "hexamer" primers. Hexamer primers are
28 generally understood to mean random (*e.g.*, non-specific primers) used in non-specific
amplification methods. (Richards Depo., Exh. 10, at 77:19 - 78:3; 133:2-9; 133:19-22.)

1 **D. The Drawings of the Patent**

2 The first pages of the '338 patent provide drawings of various methods
3 encompassed by the invention. Any drawings included in the patent are a proper reference for
4 determining claim meaning. *Wright Medical Technology, Inc. v. Osteonics Corp.*, 122 F.3d 1440,
5 1443 (Fed.Cir.1997) ("The proper construction of the claims is based upon the claim language, the
6 written description portion of the specification including any relevant drawings. . . ."); *Raleigh v.*
7 *Tandy Corp.*, 1997 WL 26299, *3 (N.D. Calif. Jan. 10, 1997) (interpreting "supporting means" as
8 requiring a flat structure; "the supporting platform ... is pictured flat in the figures depicting all
9 embodiments of the invention").

10 The first 3 drawings (Figure 1a to Figure 3) depict target capture methods alone, without
11 amplification. Figures 4, 5 and 6 depict target capture followed by amplification using only non-
12 specific primers or enzymes. The drawings included in the patent are discussed and described in
13 the text of the patent specification ('338 Patent, Exh. 8, at cols. 10 - 19.) The text of the
14 specification expressly states that in each of the drawings that include amplification (*id.*, Figures 4,
15 5 and 6) "the isolated target is *non-specifically* amplified to form a multitude of amplification
16 products." (*Id.* at col. 15, ll. 56-58, emphasis added.)

17 **E. As Used in the Claims of the '338 Patent, "Amplifying" Means Amplification**
18 **with Non-Specific Primers or Enzymes**

19 Reading the teaching, examples, and drawings included in the '338 patent
20 specification, one of ordinary skill in the art could only conclude that the term "amplifying" as
21 used in the claims means amplification methods using non-specific primers or enzymes as
22 disclosed and taught in the patent. The patent expressly teaches that sequence-specific primers are
23 not necessary. Therefore, a person of ordinary skill in the art would not understand the term
24 "amplifying" as used in the claims to encompass amplification using specific primers. Similarly,
25 based on the explicit teaching that standard, non-specific enzymes are not necessary, the ordinarily
26 skilled practitioner of the art would not understand the term "amplifying" to encompass
27 amplification using specific transcriptases and promoter sequences. The invention of the '338
28 patent cannot encompass methods that the specification states become unnecessary due to the

benefits of a target capture step prior to amplification. See *Evans Medical Ltd. v. American Cyanamid Co.*, 11 F. Supp. 2d 338, 355-56 (S.D.N.Y. 1998), *aff'd without op.*, 215 F.3d 1347 (Fed. Cir. 1999) ("There would be no quid pro quo for granting a patentee the right to exclude others from using something that his specification clearly instructs them *not* to use.").

Numerous Federal Circuit decisions demonstrate that the claims of the '338 Patent must be limited to amplification methods using non-specific primers or enzymes. Although the specification of a patent need not present every embodiment of the invention and the claims are not limited to the preferred embodiment of the invention, neither do the claims enlarge what is patented beyond what the inventor has described as the invention.

For example, in *Wang Laboratories, Inc. v. America Online, Inc.*, 197 F.3d 1377 (Fed. Cir. 1999), the patent specification described and taught only one embodiment of an invention, and the Federal Circuit held that the claims of the patent were correctly limited to that one embodiment. *Id.* at 1383. *Wang Labs* involved patent claims directed to an online information system. The accused infringer filed a motion for summary judgment of non-infringement. The outcome of the motion depended upon construction of the term "frame" as used in the patent claims. The parties agreed that the term "frame" could, in general usage, be applied to both "bit-mapped" and "character-based" displays and the specification referred generally to both types of frames. However, the examples in the patent specification described and taught character-based displays only. The district court therefore construed the term "frame" to be limited to the type of frame disclosed and described in the specification in such a manner as to constitute the invention of the patent. On appeal, the Federal Circuit affirmed.

In reaching its conclusion that the term "frame" was properly construed to be limited to the character-based displays expressly described in the specification, the Federal Circuit first found that the only systems actually described and enabled in the specification were character-based displays:

The only system that is described and enabled in the '669 specification and drawings uses a character-based protocol. The specification mentions non-character-based protocols, for example, in the "Background of the Invention" statement . . . The district court viewed the references to bit-mapped protocols as

1 *acknowledgments of the state of the art, and not as an enlargement*
2 *of the invention described in the patent.* We agree, and conclude that
3 the references to other known protocols do not describe them as
4 included in the applicant's invention, and that the specification
5 would not be so understood by a person skilled in the field of that
6 invention.

7 *Id.* at 1382 (emphasis added).

8 The Federal Circuit then held that claims could not be interpreted to have a meaning or
9 scope that would lead to their invalidity:

10 Wang argues that it is irrelevant to the construction of the claims
11 whether the specification contains an enabling description of any
12 bit-mapped decoder, stating that enablement is a requirement for
13 validity, not a factor in claim construction. However, the claims are
14 not properly construed to have a meaning or scope that would lead to
15 their invalidity for failure to satisfy the requirements of patentability.

16 *Id.* at 1382-83. The court next held that the requirements of 35 U.S.C. § 112 (written description
17 and enablement⁷) would not be met with respect to protocols other than character-based frames:

18 Although Wang is correct that a claim is not invalid simply because
19 it embraces subject matter that is not specifically illustrated, in order
20 to be covered by the claims that subject matter must be sufficiently
21 described as the applicant's invention to meet the requirements of
22 section 112. This requirement was not met as to protocols other than
23 character-based.

24 *Id.* at 1383.

25 The Federal Circuit then rejected the patentee's argument that character-based protocols
26 were simply a preferred embodiment:

27 Wang states that the character-based protocol is simply a preferred
28 embodiment and that the embodiment described in the specification
29 does not set the boundaries of the claims citing *Comark*
30 *Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1186, 48
31 USPQ2d 1117, 1124 (Fed. Cir. 1998), for its statement that
32 limitations from the specification are not to be read into the claims.
33 AOL and Netscape respond that when the subject matter that is
34 claimed is the only subject matter that is described and enabled in
35 the specification, that is the invention itself, and not simply a
36 "preferred" example of a broader invention that is not described and
37 enabled.... Whether an invention is fairly claimed more broadly than
38 the "preferred embodiment" in the specification is a question

39 ⁷ 35 U.S.C. § 112 provides in pertinent part: "The specification shall contain a written description
40 of the invention, and of the manner and process of making and using it, in such full, clear, concise,
41 and exact terms as to enable any person skilled in the art to which it pertains, or with which it is
42 most nearly connected, to make and use the same, and shall set forth the best mode contemplated
43 by the inventor of carrying out his invention."

1 specific to the content of the specification, the context in which the
2 embodiment is described, the prosecution history, and if appropriate
3 the prior art, for claims should be construed, when feasible, to
4 sustain their validity. The usage "preferred" does not of itself
5 broaden the claims beyond their support in the specification.... *The*
6 *only embodiment described in the '669 patent specification is the*
7 *character-based protocol, and the claims were correctly interpreted*
8 *as limited thereto.*

9 Id. at 1382 (emphasis added), citing *Modine Manufacturing Co. v. United States International*
10 *Trade Commission*, 75 F.3d 1545, 1551 (Fed. Cir. 1996), the court explained that "when the
11 'preferred embodiment' is described as the invention itself, the claims are not entitled to a broader
12 scope than that embodiment." 197 F.3d at 1383.

13 *Wang Labs* is directly analogous to the facts in this case. Both cases involve a summary
14 judgment motion of non-infringement. Both cases involve a claim term that could be construed
15 narrowly based on the patent specification or more broadly based on general usage. In *Wang Labs*,
16 the claim term "frame" had a meaning in general usage that encompassed both bit-mapped and
17 character-based protocols and the "Background of the Invention" section contained references to
18 support that meaning. In this case, too, the term "amplifying" has a meaning in general usage that
19 might encompass both specific and non-specific amplification.

20 Both *Wang Labs* and the instant case involve specifications that describe and teach only
21 one aspect or embodiment of the claim term at issue. In *Wang Labs*, the specification described
22 and taught only character-based display frames. While there were references in the specification
23 to other types of frames, the court found that these were not described in such a way as to be
24 included in the applicant's invention. Similarly, in the instant case, the specification describes and
25 teaches only non-specific amplification. Indeed, the specification states that the ability to use non-
26 specific primers and enzymes is a primary benefit of the '338 invention. Here, too, as in *Wang*
27 *Labs*, the patent obviously does not "enable" an invention that it does not describe, and the claims
28 should not be construed in such a manner as to render them invalid for lack of enablement. Thus,
the holding in *Wang Labs* is particularly applicable to this motion for summary judgment, and the
term "amplifying" as used in the claims of the '338 patent must be limited to non-specific
amplification with the primers or enzymes described in the '338 specification. Any other result

1 would mean that the claims cover methods of amplification using specific primers or enzymes that
2 are not described nor taught in the '338 Patent and which the patent says can be avoided.

3 In *SciMed Life Systems, Inc. v. Advanced Cardiovascular Systems, Inc.*, 242 F.3d 1337
4 (Fed. Cir. 2001), the Federal Circuit also held that a claim term was to be construed to be limited
5 in accordance with the specific embodiments disclosed in the specification. The Federal Circuit
6 held in *SciMed Life* that the term "lumens" in certain patent claims, although not limited by the
7 claims themselves, was required to be construed to encompass only *coaxial* lumens, and not to
8 encompass "dual" or "adjacent" lumen configurations. The court based its ruling on the fact that
9 all embodiments in the patent specification were limited to coaxial lumens, and that the
10 specification highlighted that one of the advantages of the invention was the use of the coaxial
11 lumens. *Id.* at 1342-43. Likewise, in the instant case, all of the examples in the '338 patent
12 specification involving amplification are limited to non-specific amplification, and the
13 specification highlights the advantage obtained because the need for specific primers and enzymes
14 may be avoided. Therefore, just as in *SciMed*, the '338 Patent's claims must be limited to non-
15 specific amplification.

16 This conclusion is also supported by *O.I. Corp. v. Tekmar Co.*, 115 F.3d 1576 (Fed. Cir.
17 1997). *O.I. Corp.* involved the meaning of the word "passage" in a claim. The court held that the
18 term "passage" was limited to non-smooth or conical types of passages because the only passage
19 structures contemplated by the specification were non-smooth or conical:

20 All of the "passage" structures contemplated by the written
21 description are thus either non-smooth or conical. In addition, the
22 description expressly distinguishes over prior art passages by stating
23 that those passages are generally smooth-walled. OI has not
24 identified anything in the prosecution history contrary to those
statements. Therefore, we conclude that one skilled in the art
reading the claims, description, and prosecution history would
conclude that the term "passage" in claim 17 does not encompass a
smooth-walled, completely cylindrical structure.

25 *Id.* at 1581.

26 The facts of *O.I.* are analogous to the instant case. In *O.I.*, while the claim contained the
27 general term "passages," the specification described only non-smooth or conical passages.
28 Likewise, while the '338 Patent claims contain the general term "amplifying," the specification

1 describes only non-specific amplification methods and states that specially tailored primers and
2 specific enzymes are not necessary when the invention is used.

3 The case of *Kraft Foods, Inc. v. International Trading Co.*, 203 F.3d 1362 (Fed. Cir. 2000)
4 is also directly applicable to the instant case. The Federal Circuit found that the term “protecting
5 back panel” was properly construed as limited to a “relatively stiff” panel because that was the
6 only type of back panel described in the specification. 203 F.3d at 1367-69. The court reached
7 this conclusion despite the fact that other claims did not expressly contained a “relatively stiff”
8 limitation:

9 Notwithstanding Kraft’s contentions, we agree with the district court
10 that the written description and prosecution history overcome any
11 presumption arising from the doctrine of claim differentiation, and
12 thus approve the district court’s construction of claim 2’s protecting
back panel as one that must be relatively stiff. . . . With respect to
the written description, every disclosed embodiment that employs a
back panel employs one that is relatively stiff. . . .

13 *Id.* at 1368. Thus, *Kraft* provides additional support for the conclusion that the term “amplifying”
14 in the ‘338 Patent claims must be construed as meaning non-specific amplification.

15 Other decisions have similarly determined that claims terms must be determined to be
16 consistent in scope with the disclosures of the specification. *See, e.g., Netword*, 242 F.3d at 1353
17 (district court correctly construed “local server computer” to mean a local server computer that has
18 a limited database of aliases and that may request updates from a central registry computer); *Toro*
19 *Co. v. White Consolidated Industries, Inc.*, 199 F.3d 1295, 1301-02 (Fed. Cir. 1999) (“cover”
20 interpreted to encompass only permanently attached covers because specification disclosed only
21 attached covers and described advantages of unitary structure as important to the invention);
22 *Biogen, Inc. v. Berlex Labs, Inc.*, 113 F. Supp. 2d 77, 98 (D.Mass. 2000) (“cell incorporating a
23 DNA construct” limited to a cell containing the particular DNA construct specifically described in
24 the specification).

25 The analysis in these cases is directly applicable to the claim construction issue presented
26 here. At numerous points, the ‘338 specification describes the claimed invention only in terms of
27 using non-specific primers or enzymes and states that this characteristic is an advantage of the
28 invention. Read together, these portions of the specification lead to the inescapable conclusion

1 that "amplifying" would have been understood by one skilled in the art at the time the patent
2 application was filed to mean non-specific amplification using non-specific primers or enzymes.

3 **F. Extrinsic Evidence Confirms the Claim Construction**

4 In addition to the ample intrinsic evidence presented in the specification to show
5 that the investors intended to limit their invention to non-specific amplification techniques and that
6 intention is apparent to one of ordinary skill, ample extrinsic evidence exists to confirm that
7 intention and interpretation. One of the sources of information that the Court may properly
8 consider in claim construction is the declaration of an expert witness. Rule 702, Fed. R. Evid.;
9 *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 589 (1993); *Pitney Bowes*, 182 F.3d
10 at 1308-09 (Fed. Cir. 1999) (consultation of extrinsic evidence appropriate to ensure that claim
11 construction is not entirely at variance with the understanding of one skilled in the art). Gen-Probe
12 has submitted the declaration of Joseph O. Falkinham III, Ph.D., which confirms what is apparent
13 from the face of the patent: One of ordinary skill in the art would have understood the term
14 "amplifying" in the '338 patent to include only the non-specific amplification methods taught by
15 the patent. One of ordinary skill in the art would not have understood the term "amplifying" to
16 include other amplification methods that use sequence-specific primers or enzymes.

17 Testimony from one of the inventors and from other witnesses confirms this conclusion. In
18 1983 Dr. Kary Mullis invented a form of specific amplification using sequence-specific primers,
19 called the "polymerase chain reaction." Dr. Mullis received the Nobel Prize in chemistry for his
20 invention. If the inventors had intended to suggest and claim the combination of target capture
21 with specific primer methods of amplification such as PCR, it would have been easy for them to do
22 so.

23 The PCR method was first described at a scientific meeting in the summer of 1985 and was
24 published in December 20, 1985. Saiki et al., "Enzymatic amplification of beta-globin genomic
25 sequences and restriction site analysis for diagnosis of sickle cell anemia," *SCIENCE* 230:1350-54
26 (1985). Within the scientific community, PCR was immediately "big news." (Richards Depo,
27 Exh. 10, at 38:6-8.) Although the application leading to the '338 patent was filed two years after
28 the disclosure of PCR, the patent does not disclose or teach the combination of target capture with

1 amplification methods using specific primers, such as PCR.

2 While the '338 inventors could have included an example that showed the combination of
3 target capture and sequence-specific amplification (such as PCR), they instead described in the
4 specification a method that permitted scientists to *avoid* the use of sequence-specific primers. That
5 is, the inventors chose to describe their invention as an *alternative* to specific primer methods such
6 as PCR. This conclusion, which is inescapable from reading the specification, is supported by
7 testimony from the inventors concerning the nature of their invention. Inventor Jon Lawrie
8 testified that the patent was meant to cover *new* amplification methods using non-specific primers,
9 not already-known methods such as PCR:

10 Q. Can you recall any reason that a reference to PCR might have
11 been intentionally omitted from the patent application?

12 A. Yes....

13 Q. If there's no reference in the ['338] patent to combining target
14 capture with PCR, do you have any explanation as to why it is
15 not there?

16 A. I believe that it was a separate, the thought behind this [referring
17 to the '338 patent] was coming up with *new* methods of
18 amplification, not old ones.

19 Q. For the purposes of what you just said you classify PCR as an
20 old method of amplification?

21 A. PCR itself was described in the patent, issued patent [e.g., it was
22 an "old" method].

23 Q. And your understanding of the 338 patent was that it was
24 directed to other methods of amplification?

25 A. The, it was, it was directed to the methods disclosed by, you
26 know, *the methods separate from PCR*.

27 Q. Those being the methods, for example, as the methods set forth
28 in example six and seven?

A. Yes.

(Lawrie Depo., Exh. 9, at 178:19 - 180:11.)

Q. However, your recollection of why - of if there's no - your
explanation of why there might not be a reference to PCR in the
patent is that the patent wasn't intended to cover old methods of
amplification such as PCR; is that right?

1 A. The patent was intended to cover the discoveries by myself,
2 Halbert and King that there should be in some, you know,
3 disclosure back at Amoco. That's what the patent was about.
4 Why PCR was left out I can just speculate. It wasn't what we
5 came [up] with, it was in the previous, it was a previous older
6 method.

7 Q. You were looking for other things?

8 A. Yeah.

9 (Id. at 180:23 – 181:13.)

10 Dr. Lawrie's testimony explains why the inventors of the '338 patent described and taught
11 only amplification with non-specific primers or enzymes. They considered that particular
12 combination to be their invention. They believed that once "specificity" was added to the overall
13 process by the use of capture probes, it was not necessary to use specific primers or enzymes in the
14 amplification step. The combination of specific target capture and *non-specific* amplification was
15 what the inventors believed they had invented, that is what the '338 patent teaches, and that is all
16 the claims of the '338 patent -- properly construed -- encompass.

17 Although the Federal Circuit has routinely cautioned District Courts not to rely upon self-
18 serving inventor testimony to *expand* the scope and construction of patent claims, the Court and
19 other District Courts have recognized the significant evidentiary and persuasive value of extrinsic
20 evidence provided by admissions by inventors and patent owners that confirm the limited scope of
21 patent claims. For example, in *Jonsson v. Stanley Works*, 903 F.2d 812 (Fed. Cir. 1990), the
22 Federal Circuit affirmed a district court's order narrowly construing patent claims consistent with
23 the admissions against interest of the inventor. *Id.* at 818. Dr. Lawrie's testimony satisfies the
24 well-settled view of relevance in this instance. *See Components, Inc. v. Western Electric, Co.*, 52
25 F.R.D. 379, 382 (D. Me. 1971); *Canadian Ingersoll-Rand Co., Ltd. v. Peterson Products of San*
26 *Mateo, Inc.*, 350 F.2d 18, 24 (9th Cir. 1965).

27 Other evidence reinforces Dr. Lawrie's testimony. On December 15, 1989, Dr. James C.
28 Richards, the Director of Business Development and Licensing for Gene-Trak Systems, admitted
that the '338 patent encompassed only amplification with non-specific primers and explicitly
contrasted the methods of the patent with other methods of amplification using specific primers.

1 Dr. Richards' analysis was set forth in a letter to one of Gene-Trak's partners, Amoco Technology
2 Company. (See Exhibit 1)

3 Dr. Richards first discussed the fact that the pending patent application encompassed the
4 use of random, non-specific primers. He then discussed the effect of combining non-specific
5 amplification with the use of an initial target capture step. Finally, he pointedly contrasted the
6 invented method with other known methods that used specific primers or promoters (e.g.,
7 enzymes):

8 Cetus, Sibia/Salk, Biotechnica, etc. all claim **specific** primers for
9 amplification whereas the present invention claims uses of the
10 opposite, namely, **non-specific** primer or promoters.... Following
extensive washing, captured target polynucleotides could be released
and the non-specific amplification process could take place.

11 (Exhibit 1 at page 2, emphasis in original).

12 At the time he wrote this letter, Dr. Richards held a Ph.D. in Microbiology and
13 Biochemistry from Southern Illinois University. (Richards Depo., Exh. 10, at 7:17-20.) He had
14 worked at Amoco from February 1984 to October 1986, when he moved to Gene-Trak. (*Id.* at
15 28:1 - 29:2-4.) At Amoco, Dr. Richards worked with the four inventors of the '338 patent, and
16 Dr. Lawrie had explained to him the nature of the invention that is the subject of the patent. (*Id.* at
17 30:5-11; 35:13 - 36:16.)

18 From October 1986 to December 1989 when he wrote the letter, Dr. Richards worked at
19 Gene-Trak⁸ with the four inventors. (*Id.* at 29:2-4; 41:10-12.) As Gene-Trak's Director of
20 Business Development and Licensing, Dr. Richards managed the company's technology assets and
21 technology needs. (*Id.* at 44:18 - 45:9.) As part of his job, Dr. Richards evaluated numerous
22 technologies and participated in licensing negotiations. (*Id.* at 47:22 - 48:24.)

23 When presentations on patent matters, including target capture patents, were made to the
24 Gene-Trak partnership committee and to the Gene-Trak scientific advisory board, Dr. Richards
25 made those presentations. (*Id.* at 60:8-13; 82:3-6; 150:9-14; 151:1-4.) Dr. Richards was a member
26 of the Gene-Trak patent committee and discussed patents with Gene-Trak's patent counsel. (*Id.* at

27
28 ⁸ Gene-Trak was a partnership formed by Amoco and Integrated Genetics in the summer of 1986.
Gene-Trak Systems became Vysis in 1991.

1 150:15-21.)

2 When Dr. Richards wrote his December 1989 letter, his sources of knowledge about the
3 application for the '338 patent were discussions he had held about the patent application with Tony
4 Janiuk, Gene-Trak's patent counsel, and with inventor Dr. Jon Lawrie. (*Id.* at 152:5-13; 186:11-
5 21.) In his December 1989 letter to senior management, Dr. Richards tried to be as accurate as
6 possible, and he has never since concluded that the way he described the invention was inaccurate.
7 (*Id.* at 154:9 - 156:12; 164:17-22; 165:14-19.) Dr. Richards' letter makes clear that the invention
8 of the '338 patent was the use of target capture *with non-specific amplification*, in express contrast
9 to methods that use specific primers or enzymes.

10 **G. Conclusion: The Claims Cover Only Target Capture Combined With Non-**
11 **Specific Amplification**

12 The interpretation to be given a term in a patent claim can only be determined and
13 confirmed with a full understanding of what the inventors actually invented and intended to
14 include within the claim. *Wang Labs*, 197 F.3d at 1384; *Renishaw*, 158 F.3d at 1250. An inventor
15 is entitled to claim only the invention described in the specification. Claims in a patent may not be
16 validly construed to be broader than the supporting disclosures of the specification. *Gentry*
17 *Gallery, Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479-80 (Fed. Cir.1998).

18 The written description of the invention set forth in the patent specification is used to
19 determine what a person skilled in the art would conclude the inventor had actually invented.
20 *Markman*, 52 F.3d at 979. The claim construction that most naturally aligns with the patent's
21 description of the invention will be, in the end, the correct construction. *Renishaw*, 158 F.3d at
22 1250.

23 In this case, the patent specification describes the invention of a method that combines
24 target capture with non-specific amplification. The patent specifically teaches, as a primary
25 benefit of the invention, that "specially tailored primers are not necessary" and that the "same
26 standard amplification reagents can be used, regardless of the targets." Each of the examples and
27 each of the drawings describes only amplification methods that use non-specific primers or
28 enzymes. The inventors clearly taught that by adding specificity to a nucleic acid assay in the

1 target capture step, they had enabled scientists to avoid the use of specific primers and enzymes in
2 the amplification step of the assay.

3 Under these circumstances, one of ordinary skill in the art as of December 1987 would
4 have understood from the specification that the inventors' method combined target capture and
5 non-specific amplification. This conclusion is reinforced by Dr. Lawrie's testimony that the
6 invention was intended to provide new alternatives to sequence-specific amplification methods,
7 such as PCR. This conclusion is made unavoidable by Dr. Richards' December 1989 description
8 of the invention, in which he expressly contrasted the invention with other methods that use
9 specific primers or promoters.

10 **IV. GEN-PROBE IS ENTITLED TO SUMMARY JUDGMENT THAT ITS TMA**
11 **PRODUCTS DO NOT LITERALLY INFRINGE THE CLAIMS OF THE '338**
12 **PATENT**

13 After the claims have been construed, the next step in an infringement analysis is the
14 comparison of the claims to the product at issue. *Carroll Touch, Inc. v. Electro Mechanical Sys.,*
15 *Inc.*, 15 F.3d 1573, 1576 (Fed.Cir. 1993). Here, Gen-Probe moves for summary judgment only on
16 the issue of literal infringement. Literal infringement of a claim requires that the accused device
17 contain each and every limitation of the claim. *Bayer AG v. Elan Pharm. Research Corp.*, 212
18 F.3d 1241, 1247 (Fed. Cir. 2000). If even one claim limitation is absent from the product at issue,
19 there can be no literal infringement as a matter of law. *See Mas-Hamilton Group v. LaGard, Inc.*,
20 156 F.3d 1206, 1211 (Fed. Cir. 1998).⁹

21 In this case, Gen-Probe's HIV-1/HCV Assay use a target-specific amplification technology
22 called Transcription-Mediated Amplification (TMA). (Longiaru Declaration, ¶5.) TMA uses
23 *specific* primers, *specific* promoters, and a *specific* polymerase enzyme that recognizes only those
24 promoters. Gen-Probe's product does not use non-specific amplification. (*Id.* at ¶¶ 6-11.) Thus,
25 the Gen-Probe product is not covered by the '338 Patent claims, which encompass only

26 ⁹ Notwithstanding the absence of literal infringement and the foregoing evidence that the inventors
27 did not intend to claim and certainly did not invent specific amplification techniques, Vysis may
28 yet contend that Gen-Probe's TMA products infringe the claims of the '338 patent under the
doctrine of equivalents. As noted here, however, Gen-Probe has expressly limited the scope of this
motion and the Court's order to the issue of literal infringement. If necessary, Gen-Probe will
address the issue of the doctrine of equivalents separately.

1 non-specific amplification. Accordingly, as a matter of law Gen-Probe's use, manufacture and
2 sale of this product are not within any of the claims of the '338 Patent. *See Mas-Hamilton*, 156
3 F.3d at 1211.

4 **V. CONCLUSION**

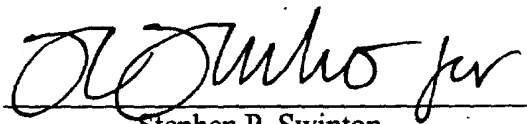
5 For the foregoing reasons, the Court should enter partial summary judgment on Counts One
6 and Three confirming that Gen-Probe's HIV-1/HCV Assays do not literally infringe the claims of
7 the '338 patent.

8
9 April 30, 2001

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22 UNITED STATES DISTRICT COURT
23 SOUTHERN DISTRICT OF CALIFORNIA

24 GEN-PROBE INCORPORATED,

25 Plaintiff,

26 v.

27 VYSIS, INC.,

28 Defendant.

No. 99CV2668H AJB
JUDGE MARILYN L. HUFF

SEPARATE STATEMENT OF UNDISPUTED FACTS
IN SUPPORT OF PLAINTIFF GEN-PROBE
INCORPORATED'S MOTION FOR PARTIAL
SUMMARY JUDGMENT

DATE: May 29, 2001
TIME: 10:30 a.m.
DEPT.: Courtroom 1

Plaintiff Gen-Probe, Incorporated respectfully submits the following statement of undisputed material facts, together with references to supporting evidence, in support of its motion for partial summary judgment.

///

UNDISPUTED MATERIAL FACTS:**SUPPORTING EVIDENCE:**

1. United States Patent No. 5,750,338 (the '338 patent) consists of the specification, including drawings, and the claims. The '338 patent contains six independent claims (claims 1, 7, 19, 27, 28 and 34). Each of these claims is generally directed to a method of, or a kit for, amplifying and/or detecting a target polynucleotide (i.e., a nucleic acid), wherein the target is first isolated on a support.

'338 Patent, Exhibit 8¹

2. Each of the claims contains a step of "amplifying" the target polynucleotide or sample. For example, claim 1 provides:

'338 Patent, Exhibit 8 at col. 32, ll. 27 to 32, (emphasis added).

1. A method for amplifying a target polynucleotide contained in a sample comprising the steps of:

(a) contacting the sample with a first support which binds to the target polynucleotide;

(b) substantially separating the support and bound target polynucleotide from the sample; and

(c) amplifying the target polynucleotide.

3. The '338 patent specification sets forth seven examples of the methods taught by the inventors. The first three examples refer only to methods of target capture alone, and do not

'338 Patent, Exhibit 8, at col. 30, ll. 14-18, (emphasis added).

¹ Unless otherwise specified, all references to Exhibits shall refer to the exhibits attached to the Notice of Lodgment of Exhibits filed concurrently herewith.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
<p>5. The '338 patent specification sets forth four examples of the amplification methods contemplated by the inventors (Examples 4-7). Consistent with the teaching of the patent that sequence-specific primers and specific enzymes are not necessary, each example suggests and describes amplification methods that use only non-specific primers and enzymes.</p>	<p>'338 Patent, Exhibit 8, at col. 30, ll. 44-45.</p>
<p>6. Example 4 illustrates "the use of RNA polymerase to amplify target DNA." It describes a method for amplifying the capture DNA by non-specific amplification using polymerases that lack transcriptional specificity.</p>	<p>'338 Patent, Exhibit 8, at col. 30, l. 59 to col. 31, l. 17.</p>
<p>7. Example 4 discloses only non-specific amplification:</p>	<p>Lawrie Depo., Exhibit 9 at 231:7-13, emphasis added.</p>
<p>8. Example 5 describes a non-specific amplification method in which the target DNA is replicated using random (<i>i.e.</i>, non-specific) primers and non-specific transcription of that DNA into RNA:</p> <p style="padding-left: 40px;">In this example, both non-specific replication of target DNA and transcription of that DNA are used to amplify capture target DNA... .. Because the primers are <i>random</i>, some will, simple (<i>sic</i>) as a matter of statistics, bind to and cause replication of sample sequences, no matter what those sequences are</p>	<p>'338 Patent, Exhibit 8, at col. 31, l. 24-54, emphasis added.</p>

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
9. Example 5 discloses only non-specific amplification.	Lawrie Depo., Exhibit 9, at 231:14-16; Richards Depo., Exhibit 10, at 139:23 – 140:3.
10. Example 6 describes replication of target DNA using DNA polymerase and <i>random</i> hexamer oligonucleotides “to bring about <i>non-specific</i> double-stranded DNA synthesis” using a series of repeated heat denaturation and enzyme replacement steps	‘338 Patent, Exhibit 8, at col. 31, l. 3 to col. 32, l. 19.
11. Example 6 discloses only <i>non-specific</i> amplification.	Lawrie Depo., Exhibit 9, at 231:17-19; Richards Depo., Exhibit 10, at 140:9-13.
12. Example 7 describes <i>non-specific</i> amplification using an RNA polymerase, Q β replicase: In this example, rRNA and RNA transcribed from target DNA is purified using a capture probe, described above. The hybrid duplex is then denatured and single stranded nucleic acids are then replicated <i>non-specifically</i> using Q β replicase...	‘338 Patent, Exhibit 8, at col. 32, l. 10-19.
13. Example 7 discloses only nonspecific amplification.	Lawrie Depo., Exhibit 9, at 231:20–22; Richards Depo., Exhibit 10, at 141: 3-7.
14. The first pages of the ‘338 patent provide drawings of various methods encompassed by the invention.	‘338 Patent, Exhibit 8.
15. The first 3 drawings (Figure 1a to Figure 3) depict target capture methods alone, without amplification.	‘338 Patent, Exhibit 8.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
16. Figures 4, 5 and 6 depict target capture followed by amplification using only non-specific primers or enzymes.	'338 Patent, Exhibit 8.
17. The drawings included in the patent are discussed and described in the text of the patent specification	'338 Patent, Exhibit 8, at cols. 10 - 19.
18. The text of the specification expressly states that in each of the drawings that include amplification (Figures, 4, 5 and 6) "the isolated target is <i>non-specifically</i> amplified to form a multitude of amplification products."	'338 Patent, Exhibit 8. at col. 15, ll. 56-58, emphasis added.
19. One of ordinary skill in the art would have understood the term "amplifying" in the '338 patent to include only the non-specific amplification methods taught by the patent.	Falkinham Declaration at ¶¶ 5 - 52.
20. One of ordinary skill in the art would not have understood the term "amplifying" to include other amplification methods that use sequence-specific primers or enzymes.	Falkinham Declaration at ¶ 5.
21. The PCR method was first described at a scientific meeting in the summer of 1985 and was published in December 20, 1985.	Saiki et al., "Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia," SCIENCE 230:1350-54 (1985).
22. Within the scientific community, PCR was immediately "big news."	Richards Depo, Exhibit 10, at 38:6-8.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
<p>23. The patent was meant to cover <i>new</i> amplification methods using non-specific primers, not already-known methods such as PCR.</p>	<p>Lawrie Depo., Exhibit 9, at 178:19 - 180:11; 180:23 - 181:13.</p>
<p>24. On December 15, 1989, Dr. James C. Richards, the Director of Business Development and Licensing for Gene-Trak Systems, admitted that the '338 patent encompassed only amplification with non-specific primers and explicitly contrasted the methods of the patent with other methods of amplification using specific primers. Dr. Richards' analysis was set forth in a letter to one of Gene-Trak's partners, Amoco Technology Company.</p>	<p>Exhibit 1</p>
<p>25. Dr. Richards first discussed the fact that the pending patent application encompassed the use of random, non-specific primers. He then discussed the effect of combining non-specific amplification with the use of an initial target capture step. Finally, he pointedly contrasted the invented method with other known methods that used specific primers or promoters (e.g., enzymes):</p> <p style="padding-left: 40px;">Cetus, Sibia/Salk, Biotechnica, etc. all claim specific primers for amplification whereas the present invention claims uses of the opposite, namely, non-specific</p>	<p>Exhibit 1 at p. 2 (emphasis in original).</p>

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
primer or promoters.... Following extensive washing, captured target polynucleotides could be released and the non-specific amplification process could take place.	
26. Gen-Probe's HIV-1/HCV Assay use a target-specific amplification technology called Transcription-Mediated Amplification (TMA).	Longiaru Declaration at ¶ 5.
27. TMA uses <i>specific</i> primers, <i>specific</i> promoters, and a <i>specific</i> polymerase enzyme that recognizes only those promoters.	Longiaru Declaration at ¶¶ 6-11.
28. Gen-Probe's product does not use non-specific amplification.	Longiaru Declaration at ¶¶ 6-11.

Dated: April 30, 2001

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13
14 UNITED STATES DISTRICT COURT
15 SOUTHERN DISTRICT OF CALIFORNIA

16
17 GEN-PROBE INCORPORATED,
18 Plaintiff,
19 v.
20 VYSIS, INC.,
21 Defendant.

No. 99-CV-2668H AJB
JUDGE MARILYN L. HUFF

**DECLARATION OF R. WILLIAM BOWEN IN
SUPPORT OF GEN-PROBE'S MOTION FOR
PARTIAL SUMMARY JUDGMENT**

Date: May 29, 2001
Time: 10:30 a.m.
Dept: Courtroom 1

22
23
24
25 I, R. William Bowen, declare as follows:


26 1. I am a member of the State Bar of California and admitted to practice before this
27 Court. I am one of the counsel of record in this action for plaintiff Gen-Probe Incorporated.

28 2. I attended the deposition of Jonathan Lawrie, Ph.D., at Raleigh, North Carolina on

1 February 15, 2001. I asked the questions and heard the responses given by Dr. Lawrie at the
2 deposition. The deposition of Dr. Lawrie was stenographically recorded and transcribed. The
3 excerpts of the Lawrie deposition set forth in Exhibit 9 to the accompanying notice of lodgment
4 are true and correct copies of the certified deposition transcript and accurately state the questions
5 and answers at the Lawrie deposition.

6 3. I attended the deposition of James Richards, Ph.D., at Waltham, Massachusetts on
7 March 30, 2001. I asked the questions and heard the responses given by Dr. Richards at the
8 deposition. The deposition of Dr. Richards was stenographically recorded and transcribed. The
9 excerpts of the Richards deposition set forth in Exhibit 10 to the accompanying notice of lodgment
10 are true and correct copies of the certified deposition transcript and accurately state the questions
11 and answers at the Richards deposition.

12 I hereby declare under penalty of perjury under the laws of the United States of America
13 that all statements made herein of my own knowledge are true and that all statements made on
14 information and belief are believed to be true. This declaration was executed by me at San Diego,
15 California on April 23, 2001.

16 
17 R. William Bowen
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